Lung Cancer UPDATES
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Iniciativa científica de:
GECP
lung cancer research

NOVEDADES EN TERAPIA DIRIGIDA

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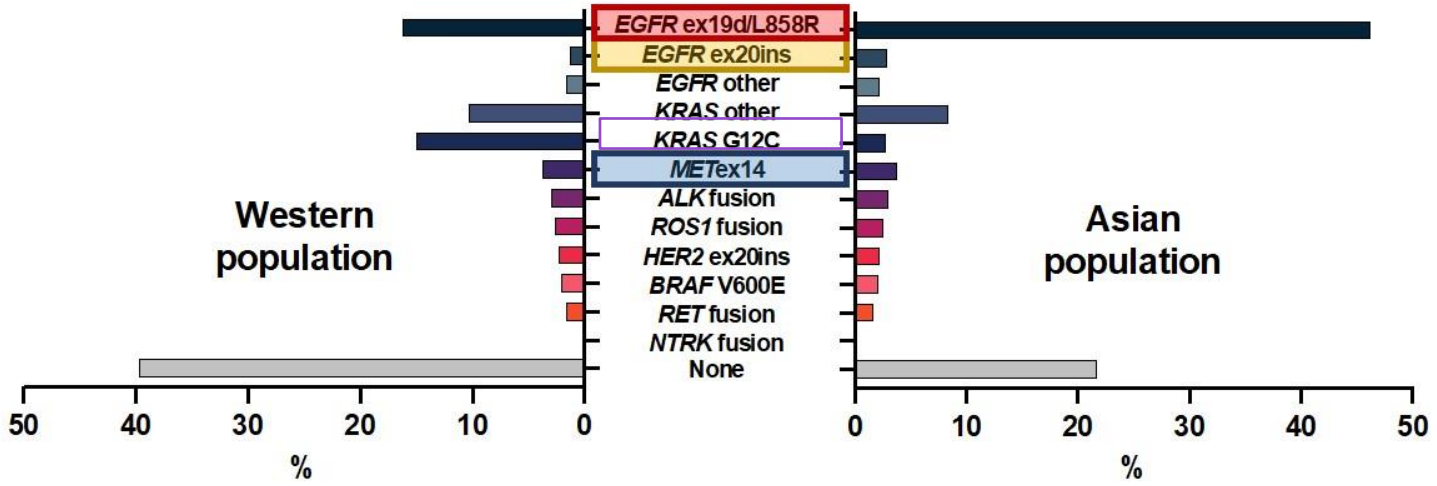
Disclosures

- Consultant or Advisory Role: Roche, Novartis, Boehringer Ingelheim, Takeda, Bristol-Myers Squibb, Sanofi
- Speaking: Roche, Merck Sharp & Dohme, Pfizer, Bristol-Myers Squibb, AstraZeneca
- Grant support: Roche, Novartis, Bristol-Myers Squibb, Pfizer, Boehringer Ingelheim, Takeda

Abstracts

- #9007: Phase (Ph) 1/2a study of CLN-081 in patients (pts) with NSCLC with *EGFR* exon 20 insertion mutations (Ins20).
- #9015: Antitumor activity of sunvozertinib in NSCLC patients with EGFR Exon20 insertion mutations after platinum and anti-PD(L)1 treatment failures.
- #9008: Amivantamab in patients with NSCLC with *MET* exon 14 skipping mutation: Updated results from the CHRYSALIS study.
- #9006: Amivantamab and lazertinib in patients with *EGFR*-mutant non–small cell lung (NSCLC) after progression on osimertinib and platinum-based chemotherapy: Updated results from CHRYSALIS-2.
- #9002: KRYSTAL-1: Activity and safety of adagrasib (MRTX849) in patients with advanced/metastatic non–small cell lung cancer (NSCLC) harboring a *KRAS*^{G12C} mutation.
- #3006: CRESTONE: Initial efficacy and safety of seribantumab in solid tumors harboring *NRG1* fusions.

Expanding list of targetable driver alterations in NSCLC



Accounts for 20-60% of our clinical practice

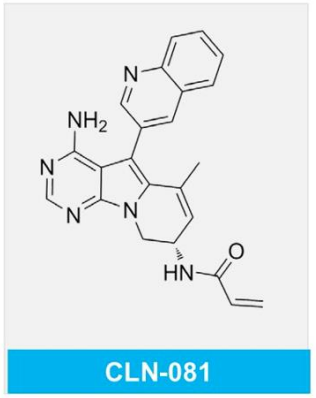
Tan AC, Tan DSW JCO 2022

Adapted from

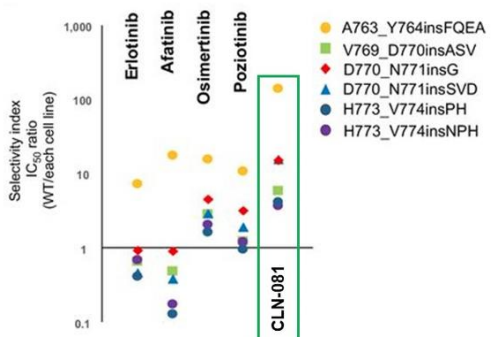
Dr Daniel SW Tan, National Cancer Centre Singapore

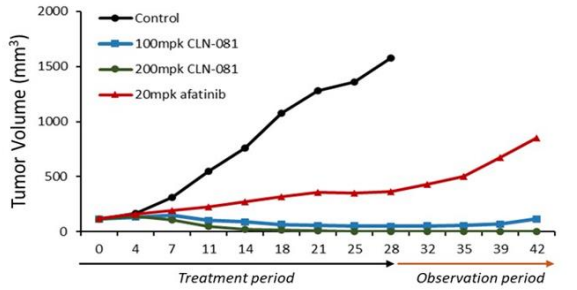
Phase 1/2a study of CLN-081 in NSCLC pts with *EGFR* ex20ins

Helena Yu, et al



Select CLN-081 pre-clinical data





LXF2478 PDX model for lung cancer harboring EGFR V769_D770INSASV

KEY ELIGIBILITY

- Confirmed recurrent or metastatic NSCLC with documented EGFR ex20ins mutation demonstrated by local laboratory
- Prior treatment in the recurrent/metastatic setting including a platinum-based chemotherapy regimen unless declined
- Prior treatment with an EGFR exon20in-targeting drug was allowed only in dose-escalation cohorts
- Patients with CNS metastases stable for ≥4 weeks prior to C1D1 were eligible

TREATMENT PLAN

- Patients receive CLN-081 twice daily and may continue to receive treatment until disease progression, unacceptable toxicity or withdrawal of consent
- Tumor response was assessed by investigators according to Response Evaluation Criteria in Solid Tumors (RECIST 1.1) at 6 weeks and every 9 weeks thereafter

PATIENT ENROLLMENT (Total N = 73)

Dose (BID)	Accelerated Titration	Rolling 6	Phase 1 Expansion	Phase 2a Expansion
30 mg	N = 2	N = 6		
45 mg	N = 1			
65 mg	N = 1	N = 6	N = 7	
100 mg	N = 1	N = 6	N = 6	N = 26
150 mg		N = 7	N = 4	

GEOGRAPHIC FOOTPRINT

Location	US	Netherlands	Singapore	Hong Kong	Taiwan
# of Sites	9	1	2	1	1

- **Data cut-off 9 May 2022**
- 73 patients enrolled across doses ranging from 30 to 150 mg BID
- Enrollment at 150 mg BID stopped after 11 patients based on toxicity

N (%)	N = 73
Treatment Ongoing	24 (33%)
Discontinued	49 (67%)
Progressive Disease	30 (61%)
Adverse Event	12 (25%)
Withdrawal of Consent	3 (6%)
Other	4 (8%)

Phase 1/2a study of CLN-081 in NSCLC pts with *EGFR* ex20ins

Helena Yu, et al

Baseline characteristics of enrolled patients

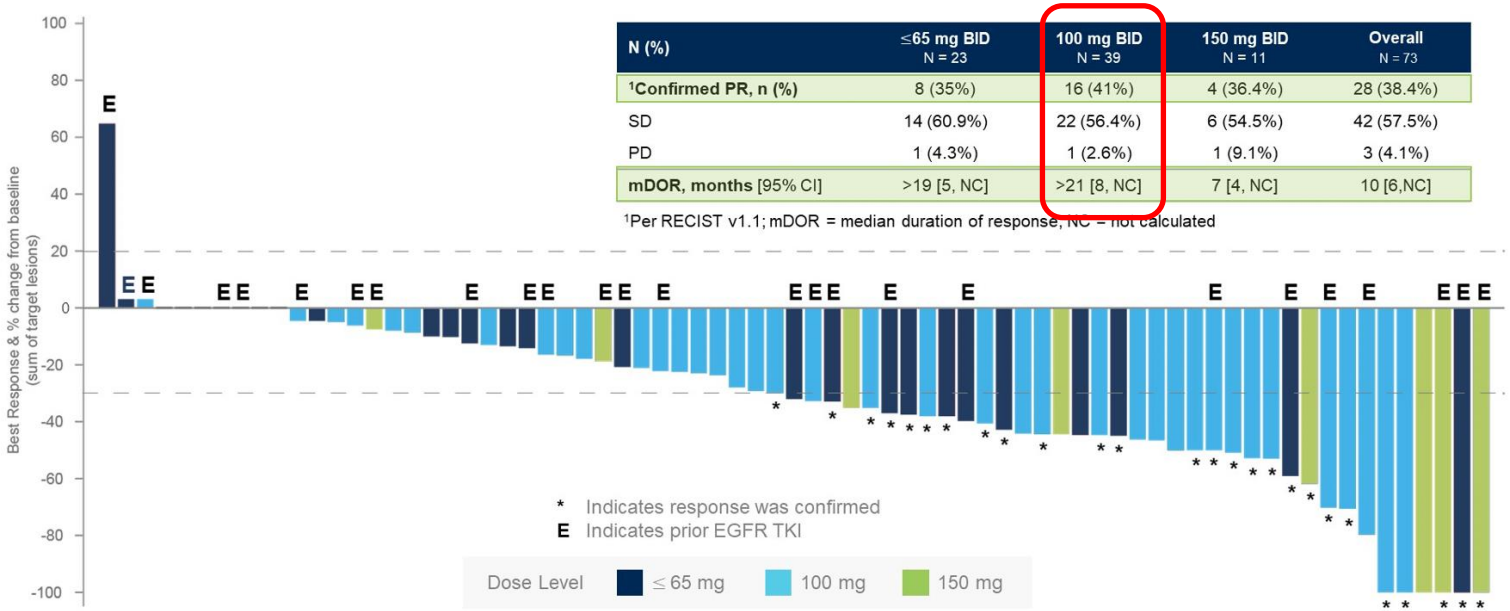
CHARACTERISTIC	ALL PATIENTS (N=73)
Median age (range)	64 (36-82)
Female	41 (56%)
ECOG PS (0, 1)	22 (30%), 51(70%)
Number of prior systemic anticancer regimens[1]	
1 (%)	22 (30%)
2 (%)	**32 (44%)**
≥3 (%)	**16 (22%)**
Median (range)	2 (1-9)
Prior EGFR TKI (non-Ex20)	**26 (36%)**
Prior afatinib or gefitinib	13 (18%)
Prior osimertinib	13 (18%)
Prior poziotinib and/or mobocertinib (%)	**3 (4%)**
Prior immunotherapy (%)	40 (55%)
History of CNS involvement (%)	**28 (38%)**

[1]Three patients with no prior therapy (declined chemotherapy)

CLN-081-001: Best percentage change from baseline in target lesion dimensions and confirmed response by dose level

N (%)	≤65 mg BID N = 23	100 mg BID N = 39	150 mg BID N = 11	Overall N = 73
[1]**Confirmed PR, n (%)**	8 (35%)	16 (41%)	4 (36.4%)	28 (38.4%)
SD	14 (60.9%)	22 (56.4%)	6 (54.5%)	42 (57.5%)
PD	1 (4.3%)	1 (2.6%)	1 (9.1%)	3 (4.1%)
mDOR, months [95% CI]	>19 [5, NC]	>21 [8, NC]	7 [4, NC]	10 [6,NC]

[1]Per RECIST v1.1; mDOR = median duration of response; NC = not calculated



Phase 1/2a study of CLN-081 in NSCLC pts with *EGFR* ex20ins

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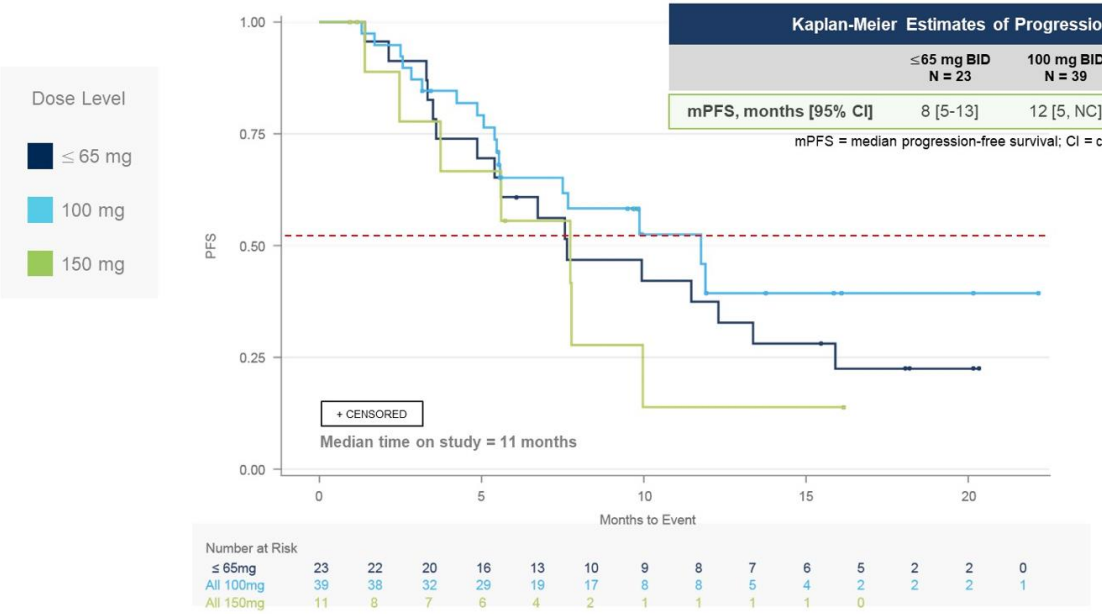


Kaplan-Meier Estimates of Progression-Free Survival

	≤65 mg BID N = 23	100 mg BID N = 39	150 mg BID N = 11	Overall N = 73
mPFS, months [95% CI]	8 [5-13]	12 [5, NC]	8 [1,10]	10 [6,12]

mPFS = median progression-free survival; CI = confidence interval; NC = not calculated

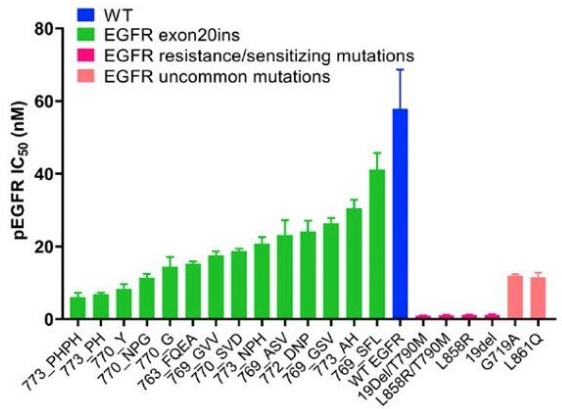
Dose BID	≤65 mg (N = 23)		100 mg (N = 39)		150 mg (N = 11)		Overall (N = 73)	
AE Term, n (%)	All grade[1]	Grade ≥ 3	All grade	Grade ≥ 3	All grade	Grade ≥ 3	All grade	Grade ≥3
Rash	19 (83)	0	32 (82)	0	7 (64)	1 (9)	58 (80)	1 (1)
Paronychia	6 (26)	0	12 (31)	0	5 (45)	0	23 (32)	0
Diarrhea	4 (17)	0	14 (36)	0	4 (36)	2 (18)	22 (30)	2 (3)
Fatigue	5 (22)	0	8 (21)	0	2 (18)	0	15 (21)	0
Anemia	7 (30)	4 (17)	5 (13)	1 (3)	2 (18)	2 (18)	14 (19)	7 (10)
Dry skin	6 (26)	0	7 (18)	0	0	0	13 (18)	0
Nausea	5 (22)	0	4 (10)	0	3 (27)	0	12 (16)	0
Stomatitis	2 (9)	0	5 (13)	0	3 (27)	1 (9)	10 (14)	1 (1)
Alopecia	3 (13)	0	6 (15)	0	0	0	9 (12)	0
Dry eye	1 (4)	0	7 (18)	0	1 (9)	0	9 (12)	0
AST increased	3 (13)	1 (4)	3 (8)	1 (3)	2 (18)	1 (9)	8 (11)	3 (4)
Decreased appetite	4 (17)	0	4 (10)	0	0	0	8 (11)	0
Dose Interruptions	5 (22)		13 (33)		6 (55)		24 (33)	
Dose Reductions	2 (9)		5 (13)		3 (27)		10 (14)	
Dose Discontinuations	2 (9)		2 (5)		2 (18)		6 (8)	

Sunvocertinib in NSCLC pts with *EGFR* ex20ins

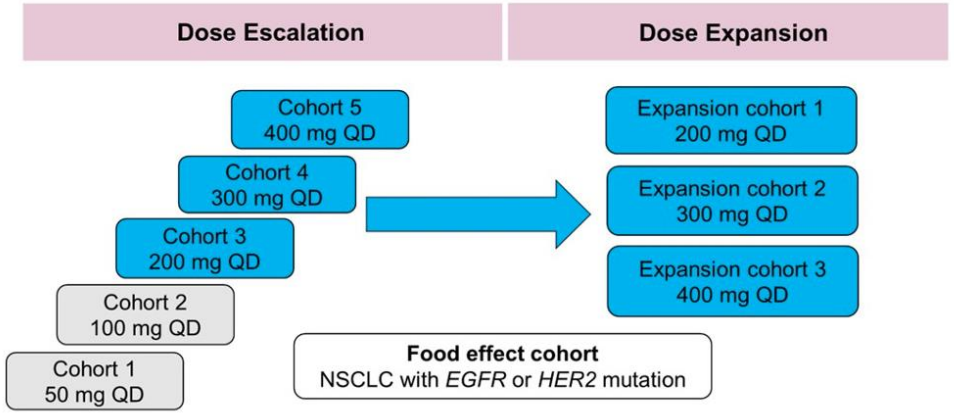
Passi Jänne, et al

Sunvozertinib is an oral, irreversible, selective EGFR TKI:

- Exon 19 deletions/L858R
- T790M
- EGFR exon 20 insertions



Phase 1 study design (WU-KONG1 and WU-KONG2 trials)



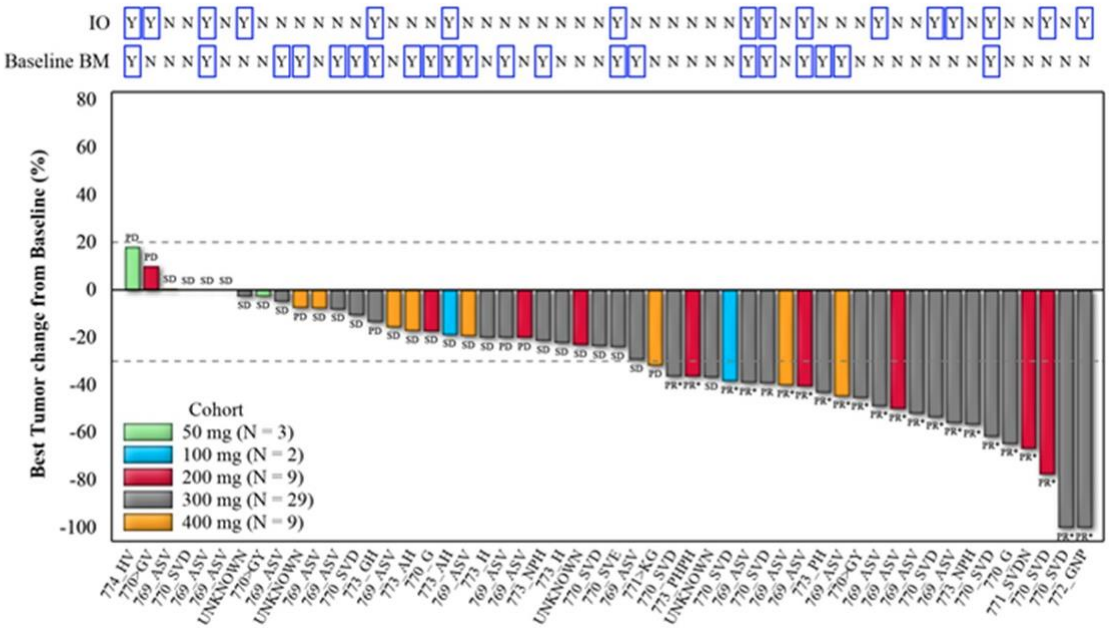
Characteristics	50 mg (N = 3)	100 mg (N = 2)	200 mg (N = 9)	300 mg (N = 29)	400 mg (N = 9)	Total (N = 52)
Median age, y (range)	48 (36-72)	58 (55-61)	61 (36-83)	59 (32-82)	54 (47-85)	59 (32-85)
Female, n (%)	3 (100.0)	1 (50.0)	7 (77.8)	15 (51.7)	5 (55.6)	31 (59.6)
Race, n (%),						
White	0 (0.0)	0 (0.0)	0 (0.0)	7 (24.1)	1 (11.1)	8 (15.4)
Asian	3 (100.0)	2 (100.0)	9 (100.0)	22 (75.9)	8 (88.9)	44 (84.6)
Previous cancer therapy						
Lines, Median (range)	5 (2-5)	4 (3-5)	3 (1-4)	2 (1-10)	1 (1-3)	3 (1-10)
Baseline BM, n (%)	1 (33.3)	1 (50.0)	2 (22.2)	13 (44.8)	4 (44.4)	21 (40.4)
Post radiotherapy, n(%)	1 (33.3)	0 (0.0)	0 (0.0)	4 (13.8)	0 (0.0)	5 (9.6)

BM: brain metastasis. Data cut-off date: 30 July, 2021.

Sunvocertinib in NSCLC pts with *EGFR* ex20ins

Passi Jänne, et al

Results	N = 52
Previous therapies median (range)	3 (1-10)
Brain Mets	21 (40%)
Prior Immunotherapy	15 (29%)
ORR (%)	40.4%
DCR. (%)	84.6%
mDOR (months)	5.9

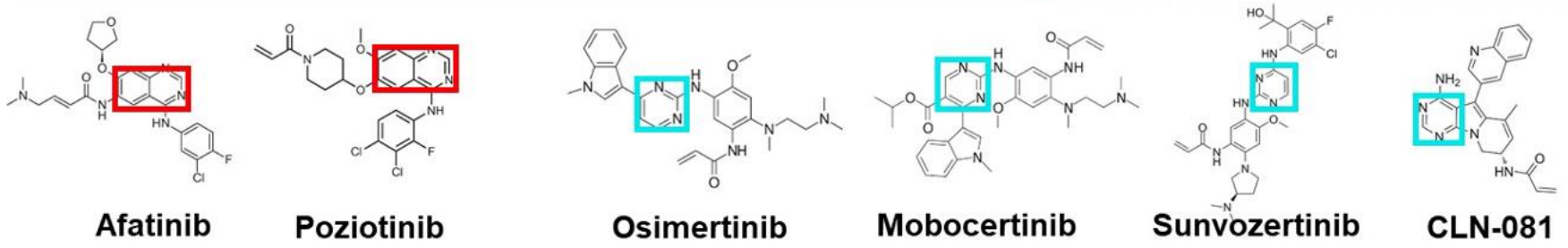


Tumor Response	50 mg (N = 3)	100 mg (N = 2)	200 mg (N = 9)	300 mg (N = 29)	400 mg (N = 9)	Total (N = 52)
Confirmed ORR, n (%)	0 (0.0)	1 (50.0)	5 (55.6)	13 (44.8)	2 (22.2)	21 (40.4)
Confirmed DCR, n (%)	2 (66.7)	2 (100.0)	7 (77.8)	26 (89.7)	7 (77.8)	44 (84.6)
Median DoR, months	NA	5.9	Not reached*	5.5	9.7	5.9

Group	PR n (%)	SD n (%)	PD n (%)	DCR n (%)
With prior anti-PD(L)1 treatment (N = 15)	8 (53.3)	4 (26.7)	3 (20.0)	12 (80.0)
Without prior anti-PD(L)1 treatment (N = 34)	13 (38.2)	17 (50.0)	4 (11.8)	30 (88.2)
Total (N = 49)	21 (42.9)	21 (42.9)	7 (14.3)	42 (85.7)

Targeting EGFR exon 20 insertions

	Drug	Class	Structure	n	ORR	PFS	DoR
	Afatinib[1] (retrospective)	Pan-HER TKI	Quinazoline-based	70	24.3%	-	11.9 m
	Poziotinib[2]	Pan-HER TKI	Quinazoline-based	115	14.8%	4.2 m	7.4 m
	Osimertinib[3,4,5]	3G EGFR TKI	Pyrimidine-based	20 (80 mg) 21 (160 mg) 24 (160 mg)	5% 24% 27%	3.6 m 9.6 m 5.5 m	- - 8.2 m
FDA Accelerated Approval	Mobocertinib[6]	EGFR TKI	Pyrimidine-based	114	28%	7.3 m	17.5 m
FDA Accelerated Approval	Amivantamab[7]	EGFR-MET Bispecific Ab	Duobody monovalent IgG1	81	40%	8.3 m	11.1 m
	Sunvozertinib[8]	EGFR TKI	Pyrimidine-based	56	41.1%	Not mature	Not mature
	CLN-081[9]	**EGFR TKI**	**Pyrimidine-based**	**73**	**38.4%**	**10 m**	**10 m**



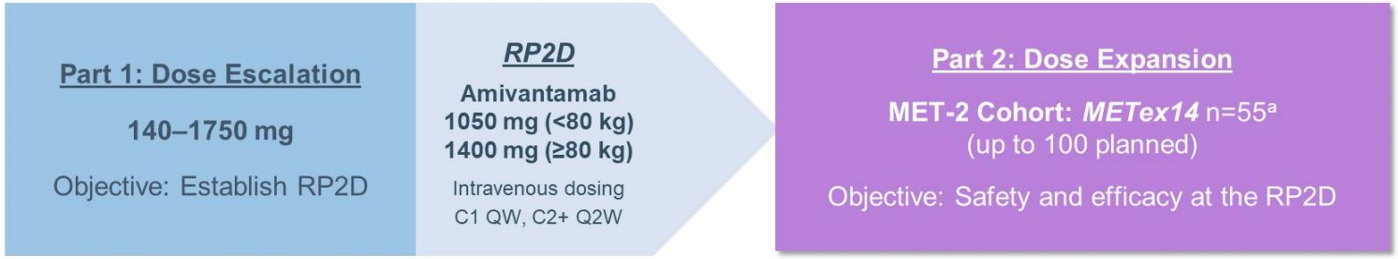
Afatinib **Poziotinib** **Osimertinib** **Mobocertinib** **Sunvozertinib** **CLN-081**

[1]Yang JC JTO 2020; [2]Le X et al, AACR 2020; [3]Veggel B et al, Ann Oncol 2018; [4]Piotrowska Z et al, ESMO 2020; [5]Zwierenga et al. ESMO 2021; [7]Zhou C et al, JAMA Onc 2021; [8]Park K et al, JCO 2021; [6]Wang et al, Can Disc 2022; [9]Yu et al ASCO 2022

PRESENTED BY:
Dr Daniel SW Tan, National Cancer Centre Singapore

Amivantamab in NSCLC pts with *MET* ex14 skipping mutation: updated results from the CHRYSALIS study

Matthew Krebs, et al



Eligibility
- Metastatic or unresectable/advanced NSCLC
- Failed or ineligible for standard of care therapy

Eligibility for METex14 Cohort
- Measurable disease
- Primary METex14 mutation by NGS of tumor or ctDNA

- As of April 11, 2022, 55 patients had been enrolled in the METex14 cohort, 28 of whom had prior MET inhibitor therapy

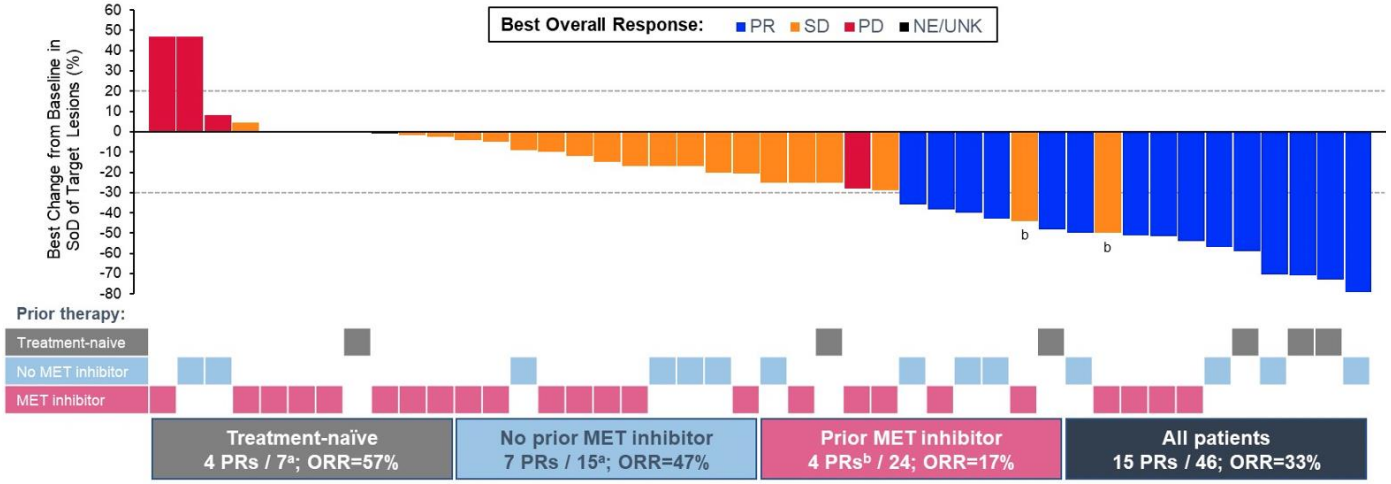
Characteristic, n (%)	Treatment-naïve, n=9	Previously-treated		Total, n=55
		No Prior MET Inhibitor,[a] n=18	Prior MET Inhibitor, n=28	
Median age, years (range)	70 (57–75)	69.5 (49–80)	70 (43–88)	70 (43–88)
Female / Male	5 (56) / 4 (44)	11 (61) / 7 (39)	16 (57) / 12 (43)	32 (58) / 23 (42)
Race				
Asian	5 (56)	9 (50)	14 (50)	28 (51)
White	4 (44)	7 (39)	10 (36)	21 (38)
Black	0	0	1 (4)	1 (2)
Not reported	0	2 (11)	3 (11)	5 (9)
History of brain metastases	1 (11)	2 (11)	**7 (25)**	10 (18)
Smoking history				
Non-smoker	4 (44)	9 (50)	16 (57)	29 (53)
Smoker	5 (56)	9 (50)	12 (43)	26 (47)
Median number of prior lines (range)	0	1.5 (1–4)	**3 (1–10)**	2 (0–10)

Amivantamab in NSCLC pts with *MET* ex14 skipping mutation: updated results from the CHRYSALIS study

Matthew Krebs, et al

Antitumor Activity of Amivantamab Monotherapy

- A total of 46 patients were efficacy evaluable



Safety Profile

TEAE (≥15%) by Preferred Term, n (%)	RP2D (n=425) Median follow-up 11.8 months		METex14 Subset (n=55) Median follow up 5.1 months	
	All Grades	Grade ≥3	All Grades	Grade ≥3
Infusion related reaction	283 (67)	11 (3)	38 (69)	3 (5)
Rash	155 (36)	8 (2)	17 (31)	1 (2)
Dermatitis acneiform	155 (36)	4 (1)	22 (40)	0
Paronychia	193 (45)	7 (2)	21 (38)	0
Fatigue	93 (22)	8 (2)	17 (31)	2 (4)
Hypoalbuminemia	135 (32)	10 (2)	15 (27)	1 (2)
Stomatitis	91 (21)	2 (0.5)	15 (27)	0
Decreased appetite	76 (18)	2 (0.5)	12 (22)	0
Dyspnea	96 (23)	21 (5)	12 (22)	4 (7)
Peripheral edema	104 (24)	4 (1)	11 (20)	0
Pruritus	79 (19)	0	12 (22)	0
Nausea	104 (24)	2 (0.5)	11 (20)	0
Constipation	105 (25)	0	10 (18)	0
Hypomagnesemia	41 (10)	0	9 (16)	0
Aspartate aminotransferase increased	64 (15)	5 (1)	9 (16)	1 (2)
Alanine aminotransferase increased	72 (17)	10 (2)	8 (15)	1 (2)
Cough	78 (18)	0	3 (5)	0

Amivantamab and lazertinib in patients with *EGFR*-mutant NSCLC after progression on osimertinib and platinum-based CT: updated results from CHRYSALIS-2

Catherine Shu, et al

Dose Expansion Cohorts

RP2CD: Lazertinib 240 mg PO +
Amivantamab 1050 mg (1400 mg for ≥80 kg) IV

- **Cohort A:** EGFR ex19del or L858R
  Post-osimertinib and platinum-based chemotherapy (n=162)
- **Cohort B:** EGFR ex20ins
  Post-standard of care and platinum-based chemotherapy
- **Cohort C:** Uncommon EGFR mutations
  Treatment naïve or post-1st or 2nd generation EGFR TKI
- **Cohort D:** EGFR ex19del or L858R
  Post-osimertinib, chemotherapy naïve, biomarker validation

Endpoints

- Overall response rate (primary)
- Duration of response
- Clinical benefit rate[a]
- Progression-free survival
- Overall survival
- Adverse events

Characteristic, n (%)	n=162
Median age, years (range)	61.5 (31–83)
Male / female	57 (35) / 105 (65)
Race	
White	42 (26)
Asian	99 (61)
Black	1 (0.6)
Not reported	20 (12)
ECOG PS 0 /1	49 (30) / 113 (70)
Brain metastases at baseline[a]	66 (41)
Untreated	30 (19)
Treated	36 (22)

Characteristic, n (%)	n=162
Smoking history	
Non-smoker	111 (69)
Smoker	49 (30)
Unknown	2 (1)
Median number of prior therapy lines (range)	3 (2–14)
2–3	117 (72)
≥4	45 (28)
Prior therapy regimens	
Frontline osimertinib → platinum-based chemo	39 (23)
1st/2nd-gen EGFR TKI → osimertinib → platinum-based chemo	67 (42)
Heavily pretreated or out of sequence	56 (35)

Amivantamab and lazertinib in patients with *EGFR*-mutant NSCLC after progression on osimertinib and platinum-based CT: updated results from CHRYSALIS-2

Catherine Shu, et al

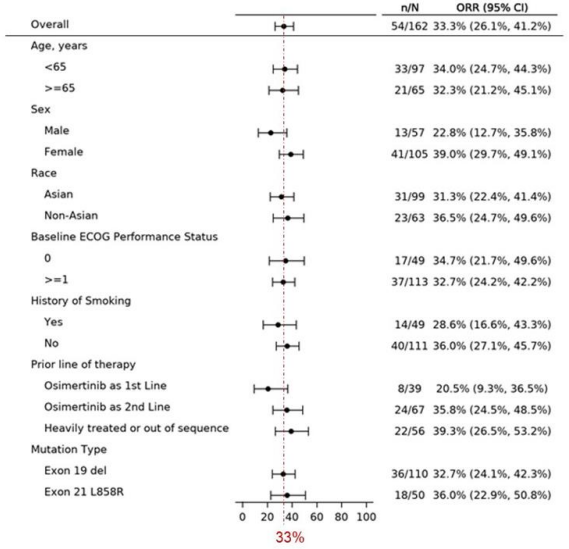
Antitumor Activity of Amivantamab + Lazertinib

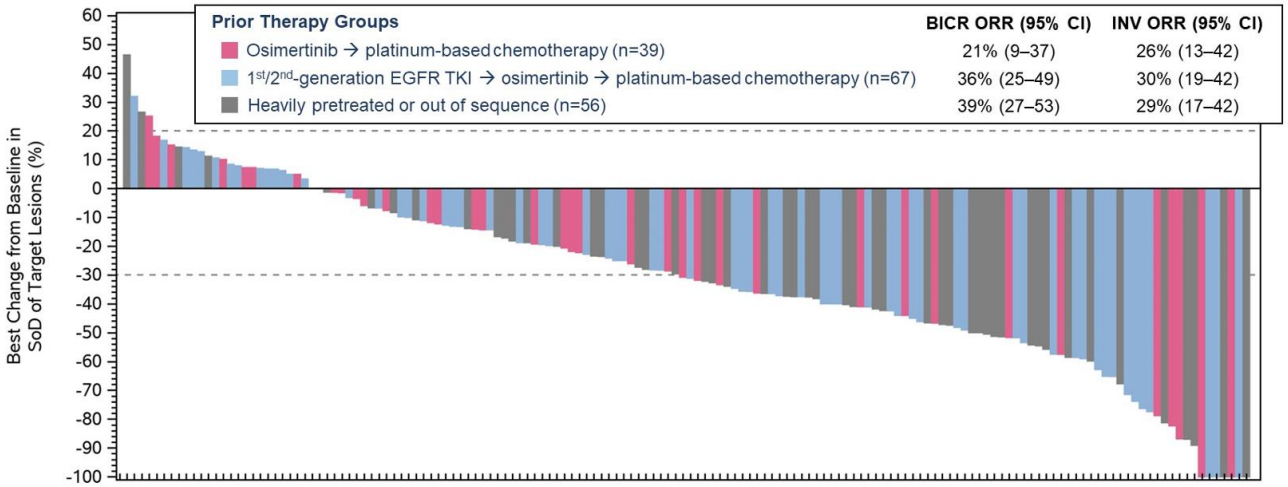
BICR-assessed Response	n=162
ORR	33% (95% CI, 26–41)
Median DOR	9.6 mo (95% CI, 7.0–NE)
Best response, n (%)	
Complete response	2 (1)
Partial response	52 (32)
Unconfirmed partial response	1 (0.6)
Stable disease	69 (43)
Progressive disease	28 (17)
NE	10 (6)
Clinical benefit rate[a]	57% (95% CI, 49–65)

Investigator-assessed ORR=28% (95% CI, 22–36)
Investigator-assessed median DOR=8.4 mo (95% CI, 5.6–NE)

Median follow-up=10.0 mo (range, 0.3–20.2)
Median progression free survival=5.1 mo (95% CI, 4.2–6.9)
Median overall survival=14.8 mo (95% CI, 12.1–NE)

[a]Percentage of patients with confirmed response or durable stable disease (duration of ≥11 weeks).
BICR, blinded independent central review; CI, confidence interval; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; mo, months; NE, not evaluable; ORR, overall response rate.





TEAEs (≥15%) by Preferred Term, n (%)	n=162 All grade	n=162 Grade ≥3
EGFR-related		
Rash	71 (44)	4 (2)
Dermatitis acneiform	55 (34)	8 (5)
Paronychia	84 (52)	6 (4)
Stomatitis	63 (39)	2 (1)
Diarrhea	36 (22)	1 (1)
Pruritus	30 (19)	1 (1)
MET-related		
Hypoalbuminemia	70 (43)	11 (7)
Peripheral edema	43 (27)	2 (1)
Other		
Infusion related reaction	108 (67)	13 (8)
Increased ALT	46 (28)	5 (3)
Nausea	40 (25)	3 (2)
Decreased appetite	39 (24)	1 (1)
Constipation	38 (23)	0
Asthenia	37 (23)	7 (4)
Dry skin	37 (23)	0
Vomiting	36 (22)	1 (1)
Increased AST	35 (22)	3 (2)
Dyspnea	33 (20)	13 (8)
Thrombocytopenia	33 (20)	2 (1)
Fatigue	32 (20)	4 (2)
Headache	29 (18)	2 (1)
Anemia	27 (17)	4 (2)
Hypocalcemia	26 (16)	1 (1)

- 10 efficacy-evaluable patients did not have any evaluable post-baseline target lesion measurements

KRYSTAL-1: activity and safety of adagrasib in pts with a/mNSCLC harboring a *KRAS*^{G12C} mutation

Alexander Spira, et al

Phase 2
NSCLC Monotherapy Treatment

Key Eligibility Criteria

- NSCLC with KRAS^{G12C} mutation[a]
- Unresectable or metastatic disease
- Prior treatment with a PD-1/L1 inhibitor in combination or in sequence with chemotherapy
- Treated, stable CNS metastases were allowed

Adagrasib 600 mg BID (Capsule, Fasted)

Study Objectives

- Primary endpoint: ORR (RECIST 1.1) per BICR
- Secondary endpoints: DOR, PFS, OS, safety

Here we report data from a registrational Phase 2 cohort evaluating adagrasib 600 mg BID in previously treated patients with NSCLC harboring a KRAS^{G12C} mutation (N=116)

Enrollment period, January 2020 to December 2020

	Adagrasib Monotherapy (N=116)[a]
Median age (range), years	64 (25–89)
Female sex, n (%)	65 (56%)
Race, n (%)	
White	97 (84%)
Black or African American	9 (8%)
Asian / Other	5 (4%) / 5 (4%)
ECOG PS, n (%)[b]	
0 / 1	18 (16%) / 97 (84%)
Smoking history, n (%)	
Never smoker	5 (4%)
Current smoker / former smoker	11 (10%) / 100 (86%)
Prior lines of systemic therapy, n (%)	
1	50 (43%)
2	40 (35%)
3+	26 (22%)
Prior platinum-based therapy and/or checkpoint inhibitor therapy, n (%)[c]	
Received prior platinum-based therapy only	2 (2%)
Received both	114 (98%)
Baseline metastases, n (%)	
Bone	46 (40%)
CNS	24 (21%)
Adrenal	22 (19%)
Liver	19 (16%)

KRYSTAL-1: activity and safety of adagrasib in pts with a/mNSCLC harboring a *KRAS*^{G12C} mutation

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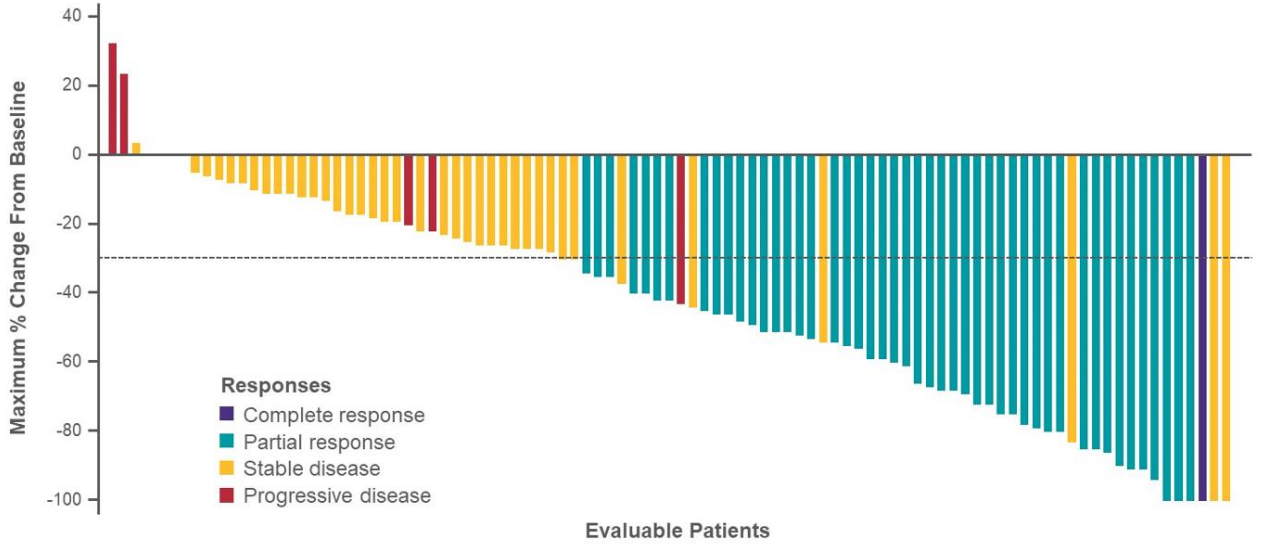
Efficacy Outcome	Adagrasib Monotherapy (n=112)[a]
Objective response rate, n (%)	48 (43%)
Best overall response, n (%)	
Complete response	1 (1%)
Partial response	47 (42%)
Stable disease	41 (37%)
Progressive disease	6 (5%)
Not evaluable	17 (15%)
Disease control rate, n (%)	89 (80%)



- Objective responses were observed in 43% (95% CI, 33.5–52.6); DCR was 80% (95% CI, 70.8–86.5)
- Responses were deep with 75% of responders achieving >50% tumor reduction

KRYSTAL-1: activity and safety of adagrasib in pts with a/mNSCLC harboring a *KRAS*^{G12C} mutation

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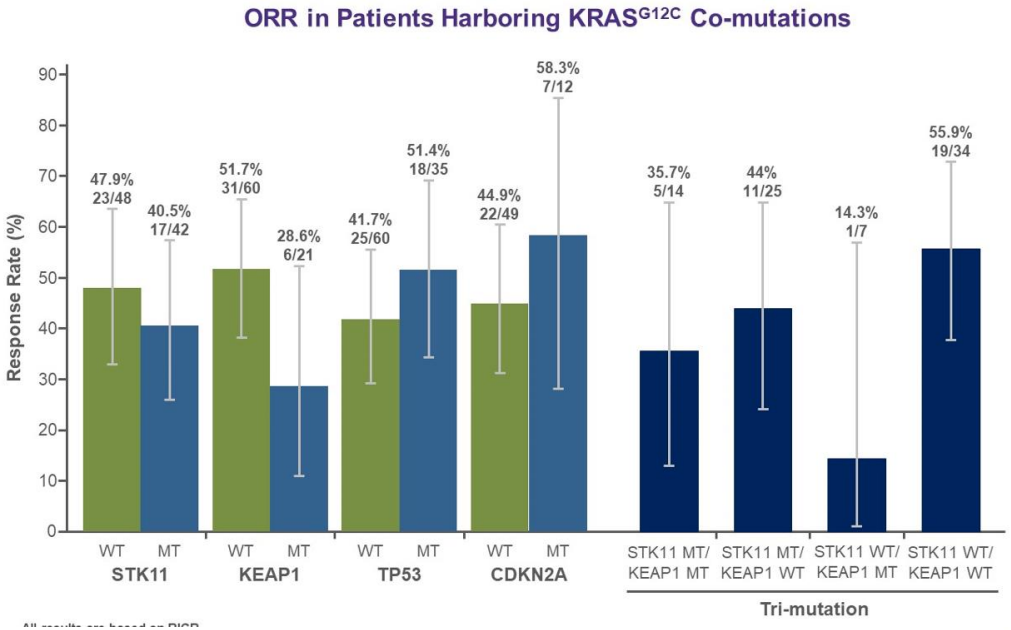
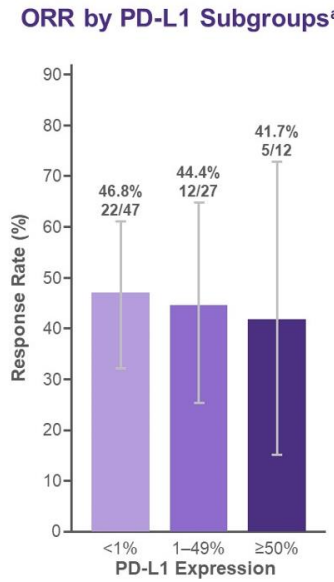




Treatment-Related Adverse Events

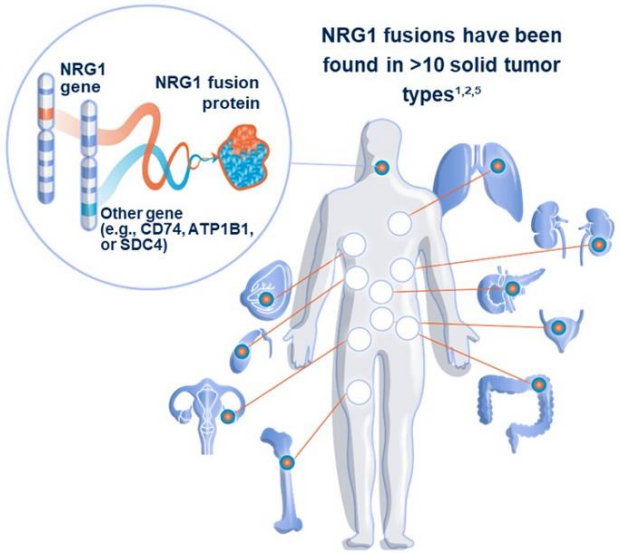
	Adagrasib Monotherapy (N=116) Capsule, Fasted	
TRAEs, n (%)	**Any Grade**	**Grades 3–4**
Any TRAEs	113 (97%)	50 (43%)
Most frequent TRAEs[a], n (%)		
Diarrhea	73 (63%)	1 (<1%)
Nausea	72 (62%)	5 (4%)
Vomiting	55 (47%)	1 (<1%)
Fatigue	47 (41%)	5 (4%)
ALT increase	32 (28%)	5 (4%)
Blood creatinine increase	30 (26%)	1 (<1%)
AST increase	29 (25%)	4 (3%)
Decreased appetite	28 (24%)	4 (3%)

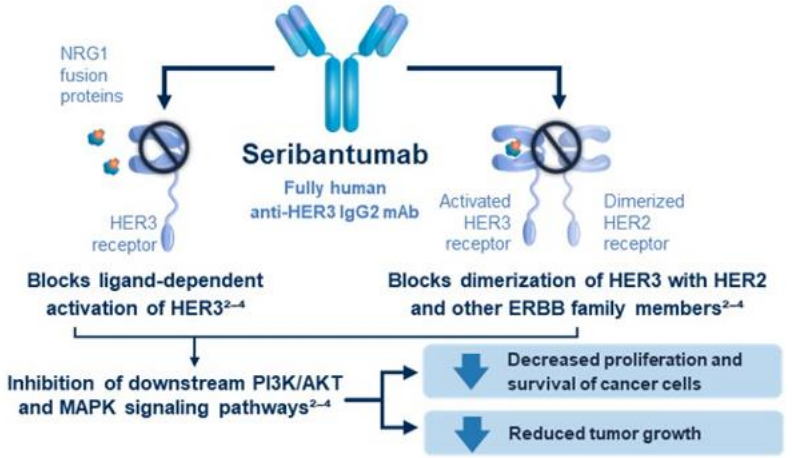
- Grade 1–2 TRAEs occurred in 53% of patients
- There were 2 grade 5 TRAEs (cardiac failure [n=1] and pulmonary hemorrhage [n=1])
- TRAEs led to dose reduction in 60/116 (52%) patients[b] and to dose interruption in 71/116 (61%) patients
- TRAEs led to discontinuation of study drug in 8/116 (7%) patients

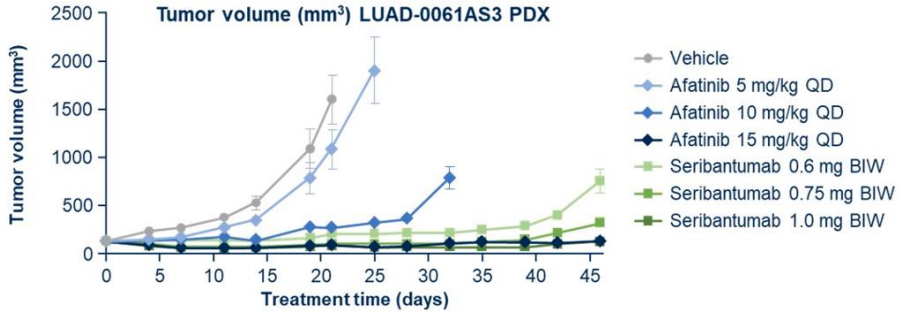
CRESTONE: initial efficacy and safety of seribantumab in solid tumors harboring *NRG1* fusions

Daniel Carrizosa, et al

- NRG1 gene fusions are:
  - Rare genomic alterations resulting from the fusion of NRG1 with a partner gene[1]
  - NRG1 fusion proteins bind to and activate HER3[1]
  - Often mutually exclusive of other known oncogenic alterations[2–4]
  - Found in 0.2% of all solid tumors;
    - Enrichment has been observed in KRAS wild-type PDAC and invasive mucinous adenocarcinoma of the lung[3–6]
- Due to the large intronic regions of the gene fusion, RNA-based sequencing is the gold standard for detecting NRG1 fusions[6–8]
- Patients with tumors harboring an NRG1 fusion have poor outcomes with standard therapies, including chemotherapy and immunotherapy[3,9]
- There are currently no approved targeted therapies for tumors harboring NRG1 fusions[6,10]







CRESTONE: initial efficacy and safety of seribantumab in solid tumors harboring *NRG1* fusions

Daniel Carrizosa, et al

#3006

Key Inclusion Criteria

- ✓ Patients with locally advanced or metastatic solid tumors harboring an NRG1 gene fusion (by local testing)
- ✓ Minimum 1 prior systemic therapy
- ✓ No other oncogenic alterations (except for Cohort 3)

Seribantumab
3g IV QW†

Cohort 1 n ≥55

No prior pan-ERBB, HER2, or HER3 targeted therapy **AND** NRG1 gene fusion centrally confirmed‡

Primary Endpoint:

- ORR by independent/central radiologic review (per RECIST v1.1)

Secondary Endpoints:

- Safety
- ORR by investigator assessment
- DOR, PFS, OS, CBR (CR, PR, SD, ≥24 weeks)

EXPLORATORY Cohort 2 n ≥10
R/R following pan-ERBB, HER2, or HER3 targeted therapy

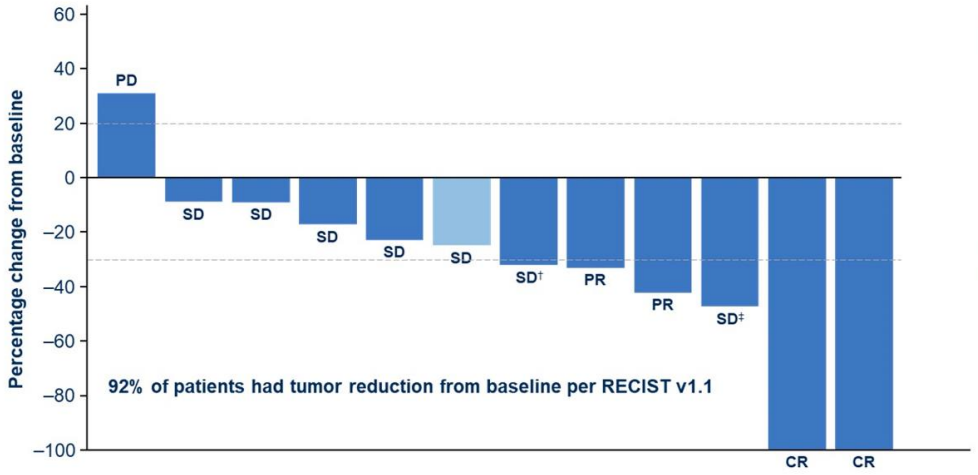
EXPLORATORY Cohort 3 n ≥10
NRG1 fusion without EGF-like domain or NRG1 fusion with other molecular alteration or insufficient tissue for confirmatory testing

Safety Population

Primary Efficacy Population

NCT04383210

Disease Characteristic	Cohort 1† (N=15)	Safety Population‡ (N=35)
Primary Tumor Type; n (%)		
Biliary Tract/cholangiocarcinoma	0	2 (6)
Breast	0	4 (11)
NSCLC	14 (93)	20 (57)
Pancreas	1 (7)	5 (14)
Other§	0	4 (11)
NRG1 Fusion Partners; n (%)		
ATP1B1	1 (7)	2 (6)
CD74	6 (40)	11 (31)
SDC4	2 (13)	2 (6)
SLC3A2	5 (33)	6 (17)
AGRN	0	2 (6)
APP	0	2 (6)
Other‖	1 (7)	10 (29)
Central NRG1 Fusion Status^; n (%)		
Confirmed	14 (93)	^
Unconfirmed	0	
Unknown^^	1 (7)	
Prior Systemic Therapies		
Median (range)	1 (1, 5)	2 (1, 6)



Confirmed INV-ORR	
Overall	33% (4/12)
NSCLC	36% (4/11)

Primary tumor type:
- Lung/NSCLC
- Pancreas

Investigator-assessed (INV) Response, %	Cohort 1 Primary Efficacy Population† (n=12‡)	Cohort 1 - NSCLC Primary Efficacy Population† (n=11‡)
Objective response rate; n (%)	**4 (33)**	**4 (36)**
Complete response; n (%)	**2 (17)**	**2 (18)**
Partial response; n (%)	**2 (17)**	**2 (18)**
Stable disease; n (%)	7 (58)	6 (55)
Progressive disease; n (%)	1 (8)	1 (9)
Disease control rate; n (%)	11 (92)	10 (91)

Lung Cancer UPDATES
ASCO HIGHLIGTHS
03-07 JUNIO 2022
Chicago, IL

Iniciativa científica de:
GECP
lung cancer research

NOVEDADES EN TERAPIA DIRIGIDA

Ivana Sullivan, MD, PhD

Hospital de la Santa Creu i Sant Pau